Adenosine-releasing silk-based brain implants for epilepsy therapy

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Rationale for therapy:
• Adenosine is an endogenous anticonvulsant of the brain that terminates seizures
• Adenosine deficiency is a pathological hallmark of epilepsy (in rodents and humans)
• Adenosine augmentation prevents pharmacoresistant seizures

Gouder et al. (2003) Epilepsia 44:877
Silk-based adenosine delivery

Anti-ictogenic and anti-epileptogenic activity of silk-based adenosine delivery

Fig. 1

Averaged daily adenosine release in vitro

Suppression of Kindled Seizures

Distinction of seizure suppression and anti-epileptogenesis

Fig. 1

IP-Status:

United States Patent 6110902
Method for the inhibition of neuronal activity leading to a focal epileptic seizure by local delivery of adenosine
Inventors: Mohler, Hanns; Boison, Detlev
Application Number: 08/881038
Publication Date: 08/29/2000
Filing Date: 06/23/1997

Silk polymer-based adenosine release: therapeutic potential for epilepsy
Inventors: Boison, Detlev; Kaplan, David L.
Application Number: PCT/US2009/044117
Publication Date: 11/19/2009
Filing Date: 05/15/2009

Development challenges:
- Pilot dose finding and safety studies in human patients using transient adenosine infusions
- Manufacturing of clinical grade implants
- Long-term delivery over months
Timelines and Milestones:

• 2010: complete preclinical studies; demonstrate efficiency in different epilepsy models; compare efficacy with standard AEDs; determine therapeutic window.
• 2010: develop clinical grade polymers for focal adenosine delivery
• 2011: pilot studies in human patients with MTLE using transient adenosine infusions; dose-finding and safety studies; seek FDA approval for clinical studies
• 2012: Phase I clinical trials using silk-based adenosine releasing intrahippocampal implants

What does the device bring to the marketplace?

• efficacy in pharmacoresistant epilepsy
• avoidance of systemic and central side effects by focal application
• exploitation of novel pharmacological principle that is based neurochemical rationale
• adenosine is already FDA approved (supraventricular tachycardia)
• silk is already FDA approved (e.g. for sutures)
• prior experience with intrathecal infusion of adenosine to treat chronic pain
• safety, because adenosine is endogenous anticonvulsant subject to rapid metabolic clearance
• potential for the prevention of epileptogenesis
• silk-based adenosine delivery is also of potential use for: chronic pain, amyotrophic lateral sclerosis, Alzheimer’s disease, autism, and schizophrenia

Funding needs:
$ 500,000.- to perform clinical pilot studies